REMARKS

According to the Office Action, prior to the present amendments, claims 1, 6-9, 21-30, 34, 36-40, 43-49, 52-, 53, and 56-63 were pending in this application. Claims 22, 34, 38-40, 43-49, 52 and 56-63 were withdrawn from consideration, and claims 1, 6-9, 21, 23-30, 36, 37 and 53 were rejected on various grounds. This listing of claims does not correspond to Applicants' record, which indicates that claim 7 has been canceled.

Claims 1, 25, 30, 36, 53, 56, 60, 61, and 63 have been amended, claims 21-24, 29, 34, 35, 38-40, 43-49, and 52 have been canceled, and new claims 64, 65 and 66 have been added. The amendments and the new claims are fully supported by the specification as originally filed and do not add new matter. Specific support for the recitation of "providing prognostic information" in claim 1 and claim 66 is at least in paragraph [0079]. All amendments and cancellations were made without prejudice or disclaimer. Applicants explicitly reserve the right to pursue any deleted subject matter in one or more continuing applications.

Election/Restrictions

Applicants note the finality of the restriction requirement communicated in the Office Action of September 21, 2006. As a result, the claims of Group I, drawn to a method of predicting the likelihood of long term survival of an estrogen receptor (ER)-positive breast cancer patient without the recurrence of breast cancer, comprising determination of the expression level of the RNA transcript of MYBL2 or its expression product, is examined in the present application.

As stated in the Office Action of September 21, 2006, although Applicants were required to select one single sequence, or a combination of sequences, in the present application, once the selected sequence(s) is/are allowable, all claims which have been limited to the allowable sequence(s) will be rejoined, and sequences containing the selected allowable sequence(s) and additional sequences will be rejoined and allowed. Accordingly, although currently claims 56-63 are indicated as being withdrawn from consideration, once base claims 1 and 25 are allowed, they should be rejoined and allowed, as a result of their dependence from claim 1 and claim 25, respectively.

Claim Objections

Claim 23 has been objected to for allegedly containing non-elected subject matter. Without acquiescing to the present objection, claim 23 has been canceled, and thus this objection is moot.

Claim Rejections – 35 USC § 102

Claims 21, 25, 26, 29 and 30 have been rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Bertucci et al. (US2003/0143539). Bertucci et al. was cited as disclosing a method comprising subjecting RNA extracted from a breast tissue obtained from a patient to gene expression analysis, determining the expression level of MYBL2, where the expression level is normalized against a control gene, and creating a report summarizing the data obtained. The Examiner specifically refers to Table 5 and Table 5A as summarizing the results of the gene expression analysis. According to the rejection, "Bertucci et al. also discloses a method of identifying genes that are related to sensitivity of anthracyclin" (Table 8). The Examiner asserts that based on the data following statistical analysis, summarized in the tables, where "a table is one form of summarizing data in a report," "one can predict the likelihood of long-term survival and treatment modality."

Claims 21 and 29 have been canceled. The rejection of claims 25, 26, and 30 is respectfully traversed.

Anticipation requires that each and every element of a claim is described in a single prior art reference, either expressly or inherently. *See* MPEP 2131 *citing Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Furthermore, the elements must be arranged as required by the claim. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990).\

Claim 25 is drawn to a method of preparing a personalized genomics profile for a patient by the following steps:

(a) subjecting RNA extracted from an estrogen receptor (ER)-positive breast tissue obtained from the patient to gene expression analysis;

(b) determining the expression level of the RNA transcript of MYBL2 or its expression product, wherein the expression level is normalized against a control gene or genes and optionally is compared to the amount found in a breast cancer reference tissue set; and

(c) creating a report summarizing the data obtained by said gene expression analysis, and containing an estimate of the likelihood of long-term survival without cancer recurrence in said patient, wherein expression of the RNA transcript of MYBL2 or its expression product is considered an indication of a decreased likelihood of long-term survival without breast cancer recurrence.

Bertucci et al. concerns a polynucleotide library useful in the molecular characterization of breast carcinoma. The library includes a pool of polynucleotide sequences wherein the sequences are either underexpressed or overexpressed in tumor cells. Of the 468 genes identified, MYBL2 is listed as SEQ ID NO: 310. Figure 1 shows that MYBL2 is differentially expressed between normal breast tissue and certain breast tumor samples. Based on this information, Table 5 lists MYBL2 as a polynucleotide sequence "interesting to distinguish a person without cancer from a cancer patient," i.e. as a polynucleotide sequence of diagnostic interest. Table 5A lists MYBL2 among the top 5 genes overexpressed in breast cancer. Table 8 lists MYBL2 among genes that are stated to be "particularly interesting to distinguish tumors sensitive to anthracycline from tumors insensitive to anthracycline. Accordingly, the only information taught about MYBL2 in these tables is its overexpression in breast cancer relative to normal breast tissue, which can be used to diagnose breast cancer, and its utility to distinguish anthracycline sensitive and insensitive tumors.

Bertucci et al. has absolutely no disclosure of step (c) recited in claim 25. Step (c) recites the creation of a report summarizing the data obtained by the gene expression analysis, and containing an estimate of the likelihood of long-term survival without cancer recurrence, wherein expression of the RNA transcript of MYBL2 or its expression product indicates a decreased likelihood of long-term survival without breast cancer recurrence.

Even if one assumes, without admission, that "a table is one form of summarizing data in a report," as the Examiner suggests (Office Action, page 3), none of the tables listing MYBL2, including Tables 5, 5A and 8, contain an estimate of the likelihood of cancer recurrence in the patient, based on an finding that the expression of the RNA transcript of MYBL2 or its expression

product indicates a decreased likelihood of long-term survival without breast cancer recurrence. As Bertucci et al. does not teach at least one step recited in claim 25, it does not anticipate the invention claimed in claim 25.

Claims 26 and 30 depend from claim 25, carrying its recitations, and are not anticipated for the same reasons.

Although it has already been established that claims 25, 26 and 30 are not anticipated by Bertucci et al., applicants note for the record that the Examiner's assertion (referring to paragraphs [0125] – [0127]) that based on the data summarized in the listed tables of Bertucci et al. "one can predict the likelihood of long-term survival and treatment modality" of the patient is in error. Paragraphs [0125]-[0127] refer to Tables 9A and 9B, stating that overexpression of genes detected by using at least one polynucleotide sequence listed in Table 9A combined with underexpression of genes detected with at least one polynucleotide sequence selected from among those included in Table 9B is indicative of "a good outcome." Accordingly, Bertucci et al. states "that a preferred DNA array according to the invention comprises at least one polynucleotide sequence selected among those included in each one of predefined polynucleotide sequences indicated in table 9A and at least one polynucleotide sequence selected among those included in each one of predefined polynucleotide sequences indicated in table 9B," and that such "DNA arrays are particularly useful to distinguish patients having a high risk (Bad Outcome) from those having a good prognosis (Good Outcome)." However, *Tables 9A and 9B do not list MYBL2*. Accordingly, Bertucci et al. has absolutely no disclosure associating MYBL2 with long-term survival, either as a single marker or in combination with other genes, and, given that MYBL2 is not listed among the genes found to be useful in distinguishing high risk patients from those having a good prognosis, one of ordinary skill would have no reason to assume or expect that MYBL2 could be used to predict the likelihood of long term survival.

Claim Rejections – 35 USC §103

Claims 23, 27 and 28 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Bertucci et al. Bertucci et al. was cited as in the previous rejection. According to the rejection, it would have been obvious to one of ordinary skill in the art to use statistical test to analyze the

expression data obtained by the method taught by Bertucci et al., and it would have been obvious to use RNA obtained from fixed paraffin-embedded biopsy sample.

The cancellation of claim 23 moots its rejection The rejection of claim 27 and 28 is respectfully traversed.

As discussed in response to the rejection under 35 U.S.C. 102(e) above, Bertucci et al. has absolutely no teaching or suggestion associating the expression level of the RNA transcript of MYBL2 or its expression product of MYBL2 with long-term survival without cancer recurrence of an ER-position breast cancer patient, as claimed in claim 25, not rejected under this section. In the absence of such teaching and suggestion, claims 27 and 28, which depend from claim 25, are not obvious over Bertucci et al. either, and the present rejection should be withdrawn.

Claim Rejections – 35 USC §112, first paragraph

Claims 1, 6-9, 21, 23, 24, 36, 37, and 53 were rejected under 35 U.S.C. 112, first paragraph, for allegedly failing to comply with the enablement requirement. The Examiner has acknowledged, however, that the specification is "enabling for a method of predicting the likelihood of long-term survival of an ER positive breast cancer patient without the recurrence of breast cancer, comprising determining the expression of the RNA transcripts of MYBL2 or its expression products in an ER positive breast cancer cell obtained from said patient, normalized against the expression level of all RNA transcripts or their products in said ER positive breast cancer cell, or a reference set of RNA transcripts or their expression products, wherein increased expression of MYBL2 relative to a reference normal tissue indicates the decreased likelihood of long-term survival without breast cancer recurrence." (Office Action, page 5)

Claims 7, 21, 23, and 24 have been canceled, which moots their rejection.

Without acquiescence to the rejection, or the reasoning underlying the rejection, claim 1 and the claims dependent thereon are now directed to the embodiment for which enablement has been acknowledged. Accordingly, the rejection of claim 1, and dependent claims 6-9, 36 and 37 should be withdrawn.

Independent claim 53, while worded differently, is also limited to ER-position breast cancer, where a conclusion of decreased likelihood of long-term survival without recurrence is drawn based on the increased expression of the RNA transcript of MYBL2 or its expression product. Accordingly, the invention claimed in claim 53 is enabled, and the rejection of claim 53 under this section should be withdrawn.

Claim Rejections – 35 USC §112, second paragraph

Claims 21, 23, 36, 37, and 53 were rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 was rejected for allegedly omitting how to determine whether the likelihood of said long term survival has increased or decreased based on the statistical analysis. Claim 23 was rejected because of its dependency on claim 21. Without acquiescence to their rejection, or the reasoning provided in support of their rejection, claims 21 and 23 have been canceled and thus their rejection is moot.

Claim 36 was rejected for its recitation of the phrase "wherein the level of the . . .comprises the RNA transcript or the product of two or more housekeeping genes." According to the rejection, it was unclear how a level can comprise genes." Claim 37 was rejected because of its dependency on claim 36. The current amendment of claim 36, which makes it clear that it is the reference set of RNA transcripts or their expression products that comprises the RNA transcript or the product of two or more housekeeping genes, is believed to obviate this rejection.

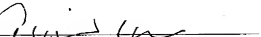
Claim 56 (should have been claim 53) was rejected for its recitation of "differential expression of MYBL2, wherein evidence of increased expression." According to the rejection, "to show an increased expression, or difference in expression, it must have some reference the sample may be compared to." Claim 53 now recites identifying evidence of differential expression of MYBL2 in a sample of a primary tumor relative to a normal breast tissue sample, which is believed to obviate this rejection.

All claims pending in this application are believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. **08-1641** referencing Attorney's Docket No: 39740-0008A.

Respectfully submitted,

Date: February 19, 2008



Ginger R. Dreger
Reg. No. 33,055

Heller Ehrman LLP
275 Middlefield Road
Menlo Park CA 94025-3506
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

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